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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,379	SWANSON ET AL.	
	Examiner	Art Unit	
	JEANINE A. GOLDBERG	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/08; 4/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed February 19, 2008 and June 16, 2008. Currently, claims 1-6 are pending.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.

3. Any objections and rejections not reiterated below are hereby withdrawn.

a. In view of the addition of the priority claim to the specification, the 102(a) rejection has been withdrawn.

Election/Restrictions

4. Applicant's election without traverse of Group 1, Claims 1-6 in the paper filed May 22, 2007 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Priority

5. This application claims priority to provisional application 60/433,045, filed December 13, 2002.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA…' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. As provided in Example 11 of the Written Description

Guidelines, no common structural attributes identify the members of the genus of "a marker within a block of linkage disequilibrium surrounding the DRD4 7R allele". The current claims encompass a large genus of nucleic acids which comprise variants in any region of any a marker within a block of linkage disequilibrium surrounding the DRD4 7R allele. The genus includes an enormous number of variants, polymorphisms and mutations for which no written description is provided in the specification. This large genus is represented in the specification by three named polymorphism for which data is provided, namely the promoter polymorphism (L1/S1), exon 1 (L2/S2) and intron 3 (G-G/A-C) polymorphisms. It is noted that the specification teaches that these polymorphisms are not in complete linkage disequilibrium with the 7R allele. This genus encompasses SNPs, deletions, insertions, translocations, microsatellites, for example. The post filing date art analyzes 103 individuals and identifies 70 SNPs/polymorphisms (see Wang et al. Am. J. Hum. Genetics, Vol. 74, pages 931-944, 2004). Table 1, as provided in Wang, provides a few exemplary polymorphisms. Of these polymorphisms, Wang specifically marks a few of the SNPs, deletions and repeats as highly linked to the 7R allele (see Table 1). The instant specification fails to provide any description of these polymorphisms and the three polymorphisms within the specification are not representative of these polymorphisms. Bhaduri teaches association of DRD4 polymorphisms with ADHD in Indian population. Bhaduri finds the exon 1 12bp duplication and exon 3 48pb VNTR in strong disequilibrium. However, Bhaduri teaches the alleles of 12bp duplication are not associated with ADHD. Thus, there is no

description of markers surrounding the DRD4 7R allele which are within linkage disequilibrium and are associated with ADHD.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a marker within a block of linkage disequilibrium surrounding the DRD4 7R allele alone is insufficient to describe the genus. There is no description of the mutational sites that exist in nature. The general knowledge in the art concerning variants does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others. The common attributes are not described. The polymorphisms shown are not representative of the genus of any a marker within a block of linkage disequilibrium surrounding the DRD4 7R allele because it is not clear which polymorphisms within the gene (coding or non-coding) region of DRD4 nucleic acid would have the same effect. One of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim. Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Response to Arguments

The response traverses the rejection. The response asserts the rejection may be based on a misunderstanding of the data provided. Upon review of the specification and the claims, the examiner has revised the written description rejection above. The claims appear to be directed to mutations outside the 7R locus which are in linkage disequilibrium with the 7R locus. As noted in the 112/2nd below, however, claim 6 does not appear to be within the scope of this genus.

The applicants correctly review the specification teaches analysis of 600 chromosomes. It is not clear that the surrounding 7R regions were analyzed. The specification does identify 56 haplotypes. The response asserts that 35 distinct DRD4 7R alleles were found. This statement does not appear to be accurate. Upon review of the 7R haplotypes of Table 1, several alleles are not represented. For example allele 35 is not represented in the 7R haplotypes. It only appears that 13 alleles from Figure 2 are represented within the 7R haplotypes. Thus applicants emphasized statement that 35 distinct DRD4-7R alleles were identified does not appear to be supported by Table 1 of the specification. Moreover, applicants do not appear to provide 35 different working examples of haplotypes. The specification only provides 13 7R haplotypes.

As discussed above, this analysis does not appear to be particularly relevant to the instant claims, because the instant claims are drawn to markers outside the DRD4 7R alleles. The instant specification names 3 markers, but these 3 markers are not in 100% linkage disequilibrium. The response asserts the specification, page 11-12, are extremely predictive of that particular allele.

- Promoter polymorphism (L1)- 90.8% of 7R alleles associated with L1 (vs 61.9% of 4R alleles)
- Exon 1 polymorphism (L2)- 93.4% of 7R alleles associated with L2 (vs 86.4% of 4R alleles)
- A-C SNP pair - 97% of 7R alleles were associated with A-C SNP pair. (A-C is associated with the DRD4 4R alleles).

The response asserts that applicants have met written description in the present case, in that a large and plainly representative sample was analyzed to identify any different 7R haplotypes. This argument has been considered but is not convincing because the claims are not drawn to 7R haplotypes. The claims are drawn to markers in linkage with the 7R haplotypes. The post filing date art analyzes 103 individuals and identifies 70 SNPs/polymorphisms (see Wang et al. Am. J. Hum. Genetics, Vol. 74, pages 931-944, 2004). Table 1, as provided in Wang, provides a few exemplary polymorphisms. Of these polymorphisms, Wang specifically marks a few of the SNPs, deletions and repeats as highly linked to the 7R allele (see Table 1). The instant specification fails to provide any description of these polymorphisms and the three polymorphisms within the specification are not representative of these polymorphisms.

Similarly, Bhaduri teaches association of DRD4 polymorphisms with ADHD in Indian population. Bhaduri finds the exon 1 12bp duplication and exon 3 48pb VNTR in strong disequilibrium. However, Bhaduri teaches the alleles of 12bp duplication are not

associated with ADHD. Thus, there is no description of markers surrounding the DRD4 7R allele which are within linkage disequilibrium and are associated with ADHD.

As noted below, Claim 6 appears to encompass DRD4 7R alleles. In the event that the claims are clarified to be directed to testing for markers within a DRD4 7R allele, the specification has describe 13 alleles within the 7R haplotypes. These 13 alleles are not representative of the genus of 7R haplotype alleles.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman.

> They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

The claims are drawn to a method of testing a patient for ADHD by testing for a marker within a block of linkage disequilibrium surrounding the DRD4 7R allele and evaluating the level of dopamine release.

The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the art

The art teaches girls and boys respond differently to the effects of exercise on children with ADHD. Tantillo et al. (Medicine and Science in Sports & Exercise, 2002, pages 203-212). Tantillo teaches that the boys and girls had different reactions to exercise with ADHD. The findings suggest an interaction between sex and exercise intensity that is not explained by physical fitness. Thus, it is unpredictable that girls and boys experience the same levels and response to stimulus.

The post filing date art analyzes the connection between yoga, and ADHD ("The effects of Yoga on ADHD" Kelley Martin, Lamar University). Martin teaches that the study presented did not support the hypothesis. Results displayed no significant difference between the treatment and non-treatment groups on both the attention problems and the hyperactivity scales (page 14). Thus, it appears that not all stimulus are statistically associated with treatment and non-treatment groups.

The art analyzes 103 individuals and identifies 70 SNPs/polymorphisms (see Wang et al. Am. J. Hum. Genetics, Vol. 74, pages 931-944, 2004). Table 1, as provided in Wang, provides a few exemplary polymorphisms. Of these polymorphisms, Wang specifically marks a few of the SNPs, deletions and repeats as highly linked to the 7R allele (see Table 1). The instant specification fails to provide any description of these polymorphisms and the three polymorphisms within the specification are not representative of these polymorphisms.

Similarly, Bhaduri teaches association of DRD4 polymorphisms with ADHD in Indian population. Bhaduri finds the exon 1 12bp duplication and exon 3 48pb VNTR in strong disequilibrium. However, Bhaduri teaches the alleles of 12bp duplication are not associated with ADHD. Thus, there is no description of markers surrounding the DRD4 7R allele which are within linkage disequilibrium and are associated with ADHD.

The art teaches genetic variations and associations are often irreproducible. Hirschhorn et al. (Genetics in Medicine. Vol. 4, No. 2, pages 45-61, March 2002) teaches that most reported associations are not robust. Of the 166 associations studied three or more times, only 6 have been consistently replicated. Hirschhorn *et al.* suggest a number of reasons for the irreproducibility of studies, suggesting population stratification, linkage disequilibrium, gene-gene or gene-environment interactions, and weak genetic effects and lack of power are possible factors that lead to such irreproducibility. Hirschhorn *et al.* caution that the current irreproducibility of most association studies should raise a cautionary alarm when considering their use as diagnostics and prognostics (p. 60, Col. 2). Thus, Hirschhorn cautions in drawing conclusions from a single report of an association between a genetic variant and disease susceptibility.

Additionally, Ioannidis (Nature Genetics, Vol. 29, pages 306-309, November 2001) teaches that the results of the first study correlate only modestly with subsequent research on the same association (abstract). Ioannidis teaches that both bias and genuine population diversity might explain why early association studies tend to overestimate the disease protection or predisposition conferred by a genetic polymorphism (abstract).

The art teaches that presence of SNPs in the same gene does not indicate that each of the genes is associated with the same diseases. Meyer et al. (PG Pub 2003/0092019), for example, teaches that SNPs in the CADPKL gene are not each associated with neuropsychiatric disorders such as schizophrenia. Specifically Meyer teaches that cadpkl5 and cadpkl6 are not associated with the disease, however cadpkl7 has a p-value of less than 0.05, therefore an association exists. Each of these polymorphisms are SNPs within the CADPKL gene, however, it is apparent that they are not all associated in the same manner with disease. Thus, Meyer exemplifies that the association of a single SNP in a gene does not indicate that all SNPs within the gene are associated with the disease.

Guidance in the Specification.

The specification provides no evidence that the full scope of the claimed invention may be practiced as broadly as claimed. The specification teaches analysis of 10 male subjects (8 Caucasian and two Hispanics). As illustrates in Figure 6, the level of dopamine is statistically different only in response to exercise at the peak time following the baseline measurement. At 30 minutes and 60 minutes the differences is not significant. Moreover, there is no indication of the 7R allele status of the various patients. There is no stratification of those ADHD patients with and without the 7R allele

or those controls with the 7R allele. Thus, it is unclear how the 7R allele factors into the analysis. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied

The claims are broadly drawn to any patient. The claims would encompass any ethnicity, any sex and adults and children. The art teaches that a study of children illustrated that girls and boys had different response to exercise (see Tantillo). Thus, within the subpopulation of children, boys and girls had different responses to exercise. The instant specification teaches the use of only boys. It is unpredictable whether girls would show the same responses. The instant specification samples boys from age 7-11 (see table 2). The specification further teaches that the alleles of the 7R varies between ethnic groups. The skilled artisan would be required to perform trial and error experimentation to practice the broad scope of the instant claims. The claims encompass any patient, children, adults, of any sex and ethnicity. The art teaches the unpredictability between these subgroups. Thus, it would constitute undue, unpredictable experimentation to practice the broad scope of the claims without further trial and error experimentation.

The claims are drawn to a method of testing for the presence of a marker within a block of linkage disequilibrium surrounding the DRD4 7R allele. The specification teaches DRD4 7R haplotypes and three markers surrounding the 7R allele which are not in complete linkage disequilibrium. The specification fails to provide any guidance

of additional markers. Wang teaches 70 SNPs have been found, only a fraction which are linked to 7R. It would require unpredictable trial and error experimentation to determine which alleles identified are in linkage disequilibrium and surrounding the 7R allele. The art, namely Meyer, teaches SNPs within the same gene, in the same block are not associated with the same diseases. Specifically Bhaduri teaches that the 12bp duplication which is in LD with the 48bp VNTR is not associated with ADHD. Thus, the skilled artisan would be unable to assume that any SNPs or variant located in proximity to the 7R alleles would be in linkage disequilibrium and encompassed within the scope of the claims.

The claims are drawn to evaluating "the level of dopamine" but fails to provide any context of level of dopamine. The specification illustrates levels on a scale of 5-25, but fails to provide any guidance which levels are indicative of ADHD and normal individuals. Inter-individual variation would be expected. Moreover, the specification illustrates that the only statistically significant difference occurred at peak exercise and not at 30 or 60 minutes following exercise. Thus, the evaluation of dopamine levels would have been unpredictable at the points after peak evaluation. Moreover, there is no indication of the 7R allele status of the various patients. There is not stratification of those ADHD patients with and without the 7R allele or those controls with the 7R allele. Thus, it is unclear how the 7R allele factors into the analysis.

The claims are drawn to any stimulus. A stimulus would broadly encompass any pin prick, fireworks, music, drug administration, yoga or smoking, for example. The specification teaches analyzing for the stimulus of exercise for dopamine levels. The art teaches that yoga is not statistically different between ADHD and non-treatment individuals. While the skilled artisan could perform further experimentation to determine whether an individual has ADHD by testing any number of stimuli including exercise,

drug administration, yoga or smoking, the results of the experimentation are unpredictable. The trial and error experimentation would amount to inventive analysis because the results of such experimentation is unpredictable given the teachings in the art.

This would require significant inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the claims broadly encompass subject matter that is not enabled in the art and specification. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized difficulties of associating alleles with phenotypes without further unpredictable and undue experimentation. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

The response traverses the rejection. The response asserts the claims are enabled according to the Wands factors. The applicant correctly identifies the issue as to whether the test for genetic polymorphisms in DRD4 and dopamine release are associated with ADHD and how.

The response asserts that there are dozens of genetic tests and the instant study of ADHD/DRD4-7R correlation analysis that was performed is the confirmatory expanded testing that provides additional statistical information to prove the correlation. This argument has been considered but is not convincing because the analysis provide in the specification do not provide any analysis of the relationship between alleles surrounding 7R and dopamine release in response to a stimulus. The specification appears to provide additional 7R alleles within 7R haplotypes and the specification separately appears to provide some analysis of dopamine release in response to exercise. This is not commensurate in scope with the instant claims.

The response asserts that the issues raised by Hirschhorn were addressed by the present invention. The response asserts that the samples were broadly selected and did not display population stratifications. This argument has been reviewed but is not convincing. The specification analyzes 10 patients, namely 8 Caucasians and 2 Hispanic, were analyzed. This is not a large sample across a representative ethnic group.

The response further argues possible linkage disequilibrium and the haplotypes issue rather unusually display minimal linkage disequilibrium in the region at issue. This argument has been reviewed but is not convincing. The response asserts that virtually

every sample in the large sample set shows complete linkage through the 7R region. This argument has been reviewed, but is not persuasive. The claims are drawn to markers "surrounding" the 7R allele, rather than within a 7R allele. Moreover, upon review in the specification, there does not appear to be complete linkage with the promoter, exon 1 or A-C SNP pair (see discussion above with regard to the written description rejection).

The response focuses on the association of 7R allele with ADHD. The claim requires analysis of both markers surrounding 7R allele and evaluating the level of dopamine. However neither the specification, nor the art appear to provide any guidance how to relate the results to ADHD. Would the absence of the marker but the presence of statistically high levels of dopamine indicate ADHD? Or the absence of the marker but the presence of low levels of dopamine? There is no guidance how to make the analysis. Similarly, there is no level of dopamine or stimulus provided. The response provides some indications of the patient's ADHD status such as normal dopamine release in children but also have the 7R allele are likely to “grow out” of many of the ADHD symptoms. Moreover, the response states that “a diagnosis of DRD4 7R in a child displaying ADHD symptoms without cognitive deficits and without a dopamine release abnormality may actually be a positive finding, as many such patients that do not display cognitive deficits can become more productive with maturity.” These correlations and indications do not appear to be in the specification or the claims. It is unpredictable based upon the specification, claims and art at the time the invention was

made how the skilled artisan would provide an indication of the patient's ADHD status based upon the method provided.

The response analyzes the Wands Factor 2 and finds "far more guidance than in Wands". This argument has been reviewed but is not persuasive. As noted above, the DRD4 7R haplotypes are not within the scope of the claim. Moreover, these are not working examples of how to test for patient ADHD status given markers surrounding a 7R allele and level of dopamine. The response asserts that "about 20 patients were analyzed for dopamine release". The Table 2 appears to analyze 10 ADHD patients for dopamine response.

The response states that the 7R allele status of the patients evaluated for dopamine release was not indicated, but is not the point of the dopamine release studies. The response then discusses a hypothesis which does not appear to be the subject of the claims. The claims are drawn to testing a patient for ADHD status by testing for a marker having a locus within a LD block surrounding a DRD4 7R allele and evaluating the level of dopamine release. There is no guidance in the specification how the skilled artisan would take the information obtained from these two experiments and provide a ADHD status. The specification does not provide any working examples where a marker surrounding a DRD4 7R allele and dopamine levels are analyzed to provide ADHD status.

The response asserts that the fifth factor considers the state of the art and all of the methods required to practice the invention are known. This argument has been

reviewed but is not convincing. It was not known at the time the invention was made how to test for ADHD status based upon a marker and level of dopamine release.

The response concludes that the present case has many working examples, various correlations between ADHD and dopamine and the DRD4 7R allele were plainly established. This argument has been reviewed but is not convincing. The specification does not provide any working examples where a marker surrounding a DRD4 7R allele and dopamine levels are analyzed to provide ADHD status.

The response states that the arguments relating to gender, specific reactions of boys and girls diagnosed with ADHD to exercise and failure in the treatment of ADHD through yoga are irrelevant. This argument has been reviewed but is not persuasive. First, the claims encompass all humans, adults and children. However, the art supports the position that girls and boys respond differently to exercise with respect to the level of dopamine release. Thus, it is unpredictable how a level of dopamine release would be standard across all genders and ages. The instant specification only appears to analyze 7-10 yr old males. This is not representative of the girls and additional ages given the teachings in the art of differences.

Moreover the response fails to address the breadth of “level of dopamine", “30, 60 minute intervals” and “stimulus" as addressed in the rejection. The specification only reviews exercise, but not stimulus generally. Further, the art teaches yoga, which is an exercise, is not correlated with dopamine levels.

As noted below, Claim 6 appears to encompass DRD4 7R alleles. In the event that the claims are clarified to be directed to testing for markers within a DRD4 7R

allele, the specification has not enabled how to use the 7R alleles with level of dopamine to make an ADHD status assessment. A similar analysis is applicable.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-6 are indefinite because it is unclear what is being claimed. Claim 1 appears to require a marker outside the 7R repeat, i.e. a locus within a block of linkage disequilibrium *surrounding* a DRD4 7R allele. Claim 6 appears to require the marker comprises the DRD4 7R allele. It is unclear whether the marker is inside the 7R repeat or outside the 7R repeat region.

B) Claim 1 requires testing for ADHD status, however the claims fail to provide how to test for the status. For example, if the results indicate that the L2 allele is present and the dopamine level is 20pg/ml, what the patient ADHD status was. Therefore, the claims are unclear how to test for ADHD status.

Conclusion

9. No claims allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

/Jeanine A Goldberg/
Primary Examiner, Art Unit 1634
September 11, 2008